Amendments to the Drawings

The Examiner has stated that the informal drawing of Figure 10 is not of sufficient quality to permit examination. Replacements Sheets of all drawings including a replacement sheet for Figure 10 in compliance with 37 CFR 1.121(d) are being filed to overcome the deficiencies in the drawings.

Attachment: Replacement Sheets

REMARKS

Claim Objections

Claims 25-43 and 51-55 have been objected to due to minor informalities. Applicant has amended these claims to overcome these informalities.

Amendments

Independent claim 22 has been amended to recite the steps of directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis; and directing a liquid through the rough filter in a direction opposite to the direction of filtration for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule. Independent claim 68 has been similarly amended.

Independent claim 50 has been amended to recite directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis. Independent claim 69 has been similarly amended.

Previously withdrawn Claims 1-21, 44-49, 56-67 and 70-71 have been canceled.

102(e) Rejections

The Examiner has rejected claims 22-31, 35, 41-43, 50-54, and 68-69 under 35 U.S.C. 102(e) as being anticipated by Burshteyn et al. (US Pub. No. 2002/0123154).

An embodiment of Applicant's device will be discussed without limitation of the claims. Applicant's Fig. 5 depicts a schematic of steps that can be included in preparing a macromolecule sample. The liquid mixture 202 contains a macromolecule 104, and can also contain fine components 213, e.g., salts, molecules smaller than the macromolecule, and the like; and rough components 207, e.g., cells, cell fragments, particulate contaminants, molecules larger than the macromolecule, and the like.

Macromolecule 104 can be dissolved in the liquid mixture, or can be partially contained in cells, as depicted. Optional lysis step 204 lyses at least a portion of the cells to release macromolecule 104.

A rough separation step 410 applies the liquid mixture to a rough filter 412, and a pressure differential across filter 412 directs at least a portion of the liquid, macromolecule 104, and the fine components 213 through the filter, separating at least a portion of rough components 207 at rough filter 412. Rough filter 412 can be selected to remove at least a portion of components that are larger than the macromolecule, e.g., greater in diameter or molecular weight. The rough filter 412 removes components that are greater in molecular weight than the molecular weight of the macromolecule by about 150%, by about 125%, by about 110%, and by about 105%. The concentration of the macromolecule is increased by in this step by at least 50%, 100%, or 200%.

A fine separation step 414 applies the liquid mixture to a fine filter 416, and a pressure differential across the filter directs at least a portion of the liquid and the fine components 213 through the filter to waste 418, separating at least a portion of macromolecule 104 at the filter. Fine filter 416 can be selected to remove at least a portion of components that are smaller than the macromolecule, e.g., salt components.

The liquid mixture that remains at the filter has a greater concentration of macromolecule 104, and a reduced concentration of soluble fine components 213, e.g., salts.

Advantageously, the filters and filtration methods employ the technique of "back-flushing." That is, each filter can be cleaned by directing a fluid, e.g., a buffer, a cleaning fluid, water, a solvent, a desalination buffer, a denaturation buffer, combinations thereof, and the like through the filter in a direction opposite to a previous filtration step. For example, once the macromolecule has gone through the rough filtration step, a liquid can be directed through the rough filter in a direction opposite to the direction of filtration. This cleans the filter membrane surface to restore it to its initial capacity and characteristics.

Also, in order to direct the macromolecule to the denaturization vessel, once the macromolecule has gone through the fine filtration step, valve 522 opens and pump 518 draws a portion of buffer from reservoir 524. Valve 522 closes, valve 510 opens, and pump 518 directs the buffer through filter 416 in a direction opposite to the direction of filtration. Preferably, pumps 518 and 506 operate cooperatively to direct the buffer through filter 416, and pump 506 then directs the mixture through valve 520. Addition of the buffer through the filter can dislodge

portions of macromolecule 104 that may become associated with fine filter 416 in the fine filtration step.

Finally, pump 506 drives the combination of macromolecule 104 to optional denaturation vessel 526, whereupon the denatured macromolecule 104' can be then directed to analysis site 106.

Burshteyn describes an apparatus and method for removing interferents from a test sample containing a mixture of a composition of interest and interferents in an automated apparatus. As shown in Burshteyn's Figures 2 and 3, the filtration device 24 includes a microporous hollow fiber membrane 60 having a plurality of pores 65 sized to retain the composition of interest while allowing smaller diameter interferents to pass through the membrane. As shown in Fig. 3, a sample of cells is shown in lumen 66 as a mixture comprising cells 74 and interferents 72. The mean diameter of the pores 65 is smaller than the diameter of the cells of interest, but greater than the diameter of interferents, thus allowing the interferent, to pass through the pores while the cells of interest, or larger diameter cells 74 remain in the lumen 66.

As shown in Figure 4G, a buffer 49 is then dispensed from the buffer reservoir 46 through the filtration device into the sample container 16. Movement of buffer through the device flushes the desired sample of cells from the lumen 66 into the sample container 16. Detergent can also be similarly run through the filtration device through the lumen 66 and to clean it after each sample, after a predetermined number of samples, or upon fouling of the membrane 60.

The Examiner states that Burshteyn describes a rough filter to separate at least a portion of rough components and a fine filter selected to separate at least a portion of the fine components. Applicant respectfully disagrees.

Burshteyn in all embodiments only describes a fine filter, wherein the filter separates components that are smaller than the desired cell sample. He nowhere describes a rough filter to separate components that are larger than the desired cell sample. Additionally, his system is not designed to incorporate a rough filter. As can be seen in FIG. 4G, the buffer reservoir 46 is connected to the membrane filter 60 to run the buffer directly through the lumen 66 and through the collected sample cells and into the sample container. The interferents are separated and are

outside of the lumen are directed to a waste site with the aid of a vacuum 30. Thus the lumen 60 is only designed to retain cells of interest, that are larger than interferent.

Thus, Burshtyn does not describe Applicant's step of applying the mixture applying to a rough filter selected to separate at least a portion of the rough components.

Further, because Burshytyn does not have a rough filter, he does not describe the step of directing a liquid through the rough filter in a direction opposite to the direction of filtration for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule.

Also, Burshtyn does not describe Applicant's steps of directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis and directing a liquid through the rough filter in a direction opposite to the direction of filtration for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule.

Burshtyn's buffer is directed through the lumen to simply push the sample into the sample container. It is not directed through the fine filter in a direction opposite to the direction of filtration. If it was, the buffer would be aimed directly through the side membrane 60, and not from the top of lumen to simply flush the sample into the container.

Independent claim 22 has been amended to recite directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis, and directing a liquid through the rough filter in a direction opposite to the direction of filtration for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule. These limitations as well as the step of applying the mixture to a rough filter selected to separate at least a portion of the rough components are not described by Burshteyn.

Independent claim 68 has also been similarly amended. Thus, claims 22 and 68, or any claim dependent on the same are allowable for at least these reasons.

Independent claims 50 and 69 have been amended to recite the step of directing a liquid through the fine filter in a direction opposite to the direction of filtration, and the macromolecule thus being directed further in the apparatus for analysis. As stated, Burshteyn does not describe

this limitation. Thus, claims 50 and 69 or any claims dependent on the same are allowable for at least these reasons.

103(a) Rejections

Dependent claims 32-34 have been rejected under 103(a) by the Examiner as being unpatentable over Burshteyn. As previously described, Burshteyn does not describe all of the limitations of independent claim 22. Thus, dependent claims 32-34 are allowable for at least this reason.

Also with regard to claim 34, the Examiner states that it would have been obvious for Burshteyn to have a filter that separates rough components that have a molecular weight greater than about 110% of the molecular weight of the macromolecule as recited in claim 34. Applicant respectfully disagrees. Burshteyn only describes a fine filter to separate components that are smaller than the desired cell sample, not a rough filter as claimed by the Applicant. Thus, claim 34 is further allowable for this reason.

Dependent claim 36 has been rejected as being unpatentable over Burshteyn in view of Holmes (US 4830969).

Holmes describes a process for the separation from other cellular materials of heat agglomeration resistant water soluble nitrogen containing organic compounds such as plasmids, RNA's, mitochondrial DNA's, viral DNA's, chloroplast DNA's, other episomal DNA's, and certain proteins. The process comprises heating cellular materials in a solution of lysing agent to lyse the desired cells and to agglomerate water soluble nitrogen containing compounds such as certain chromosomal DNA's, which are not resistant to agglomeration (Holmes, Abstract).

As stated, Burshteyn does not describe all the of the limitations of independent claim 22. Specifically, he does not describe the steps of directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis, directing a liquid through the rough filter in a direction opposite to the direction of filtration for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule, and applying the mixture to a rough filter selected to separate at least a portion of the rough

components. Holmes similarly does not describe these limitations. Thus, dependent claim 36 is allowable over Burshteyn and Holmes either alone or in combination.

Dependent claims 37-40 and 55 have also been rejected over Bursheyen in view of Shnipelsky et al (Schnipelsky, US 6645758).

Shnipelsky describes a cuvette and a method of use to prevent nucleic acid amplified by PCR technology from being released into the atmosphere, while still proceeding to a detection step to determine whether or not the nucleic acid is present (Shnipelsky, Abstract).

As stated, Burshteyn does not describe all of the limitations of independent claim 22. Similarly, Shnipelsky either alone or in combination with Burshteyn does not describe those limitations. Dependent claims 37-40 are allowable for at least these reasons.

Shnipelsky either alone or in combination with Burshtyen also does not describe all of the limitations of independent claim 50. Specifically, neither reference describes the step of directing a liquid through the fine filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis. Thus, dependent claim 55 that is dependent on claim 50 is allowable for at least this reason.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By_____
Sumedha A. Bahri
Registration No. 57,427
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Date: 01/09/08